

REMARKS

Upon entry of the amendments herein, claims 1-25 and 28 remain pending in the application. Claims 1, 5, 6 and 23 have been amended. No new matter has been introduced by any of these amendments.

I. Introduction

Applicants and the undersigned acknowledge with gratitude the time taken by Examiners Moran and Marschel to participate in a telephone interview on October 12, 2005 to discuss the outstanding issues. The amendments and remarks now presented reflect this discussion.

II. Rejection under 35 U.S.C. §101 (Nonstatutory Invention)

The claims, pending for three and one-half years at the time the present Office Action was issued, have only now been rejected under 35 U.S.C. §101 as being "directed to non-statutory algorithm type subject matter." This rejection was discussed at length during the October 12, 2005 interview.

The Examiners perceive a problem with claim 1. They expressed concern that the claim allegedly lacks a tangible result. A concluding step indicating an output of the steps then presented in the claim would, in their view, remedy the perceived defect. The Examiners also opined that the method steps then before them did not adequately relate back to the preamble.

Claim 1 has been amended to address these points and more thoroughly set forth the claimed invention. The newly added steps not only further set forth the tangible end result of the inventive method, but also point out the connection between the "backbone configurations" recited in the preamble and the "backbone configurations" that are the product of the claimed

design method. Support for the amendments to claim 1 can be found in the specification on, for example, page 8, lines 11-22; page 9, lines 14-25; and page 22, lines 17-21.

The claims have been rejected as though they were directed to a merely aesthetic or abstract mathematical exercise. This premise is fundamentally mistaken, as is the rejection it allegedly supports. The subject matter rejection, based on this flawed premise, must be withdrawn.

The rejection quoted a passage from MPEP §2106 (IV) (B) (2) (b): "For example, a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory. However, a claimed process for digitally filtering noise employing the mathematical algorithm is statutory." This example actually supports rather than undermines the patentability of the claimed invention. The invention does not simply model protein structures, but filters out those that are not designable—the "noise" in the signal. The claimed design method, which filters an astronomically large initial pool of backbone configurations, identifies and selects the useful, designable protein backbone configurations from among that pool. In so doing, it also identifies undesirable configurations. The present invention comports fully with the criterion for patentability set forth in the passage quoted by the Examiner and with all other applicable criteria.

On its face, the claimed invention is a method of identifying protein backbone configurations. Even if the use of mathematics were a basis for rejecting a patent claim, which it is not, the Examiner has failed to carry even that burden. The claimed invention is a process within the meaning intended in the statute. The process is one in which a number of steps are combined to identify and select designable protein backbone configurations and ultimately produce polypeptides with great, evident potential for use in the real world. Proteins are

tangible. Their backbone configurations, as represented, which they must be to carry out the invention, are no less tangible. Even to identify a thing itself requires the production of something tangible. Representation is a precursor to use either by a human or another machine. It is reasonable to suppose, in fact, that one might feed the output from Applicants' process, which output is not attainable via the Dahiyat process, into the Dahiyat process. Furthermore, the claimed design method allows for the immediate elimination of myriad undesirable possibilities, thus saving considerable expenditure of time, money and effort.

The Examiner's attention is drawn to the Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility ("the Guidelines") published by the Office after the telephonic interview. The Guidelines set forth criteria for determining if subject matter is statutory under 35 U.S.C. §101. The invention as claimed complies with the statute as well as the Guidelines.

The Guidelines enumerate the four statutory categories of patentable subject matter under §101. The instantly claimed **process** is clearly in one of these categories. The Guidelines further enumerate the three categories of "judicial exceptions" to subject matter that may initially be determined to fall into one of the four statutory categories. Again, the presently claimed process clearly does not fall within the categories of any of the exceptions. No prima facie case has been made by the Examiner, nor can such a case be made, that the presently claimed subject matter does not fall into one of the statutory categories or that it does fall into one of the judicial exceptions.

The Guidelines state, for example, that "[F]or eligibility analysis, physical transformation 'is not an invariable requirement....'" §IV.C.2.b., Practical Application That Produces a Useful, Concrete, and Tangible Result. Again, the presently claimed invention meets all of the

requirements for such results. Clearly, the claimed invention is useful. It enables the identification of designable protein backbone configurations and the elimination of myriad undesirable backbone configurations. The Guidelines further state: "The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing," but that such a claim must set forth "a practical application to produce a real-world result...that can be substantially repeatable or the process must substantially produce the same result again." The claimed process, as presented, complies with the Guidelines regarding utility, concreteness and tangibility.

The Guidelines were issued in the wake of a recent decision by the Board of Patent Appeals and Interferences, *Ex parte Lundgren*, Appeal No. 2003-2088 (BPAI 2005). Lundgren had claimed a "method of compensating a manager" that involved several steps of calculating a proper compensation based on performance criteria and then transferring payment to the manager. The majority opinion of the Board held such a claim to "produce a useful, concrete, tangible result" without being a "law of nature, physical phenomenon or abstract idea." There can be no question that if such a claim meets the criteria for patentability under §101, the present claims do as well.

Finally, there are many passages in the specification directed to the end results of the practice of the claimed invention, which end results must be considered useful, tangible and concrete by any criteria that may be applied in the present context. As examples, the Examiner's attention is directed to the passages on page 8, lines 17-22; page 9, lines 21-29; page 16, lines 3-5 and 9-11; page 20, lines 15-26; and page 22, lines 17 and 18.

III. Rejection under 35 U.S.C. §112, First Paragraph

The claims stand rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. The Examiner maintains new matter was introduced by Applicants in the previous claim amendments.

Although Applicants disagree and do not acquiesce in the propriety of the rejection, the language objected to by the Examiner has been deleted from the claims, and the rejection is moot. Applicants have retained the word “novel” in the preamble of the claim and have more thoroughly connected that language to the subsequently recited process steps. As discussed in the interview, configurations produced by the claimed method are novel with respect to any presently known natural or man-made protein backbone configurations.

IV. Claim Rejections under 35 U.S.C §112, Second Paragraph

The claims also stand rejected under U.S.C §112, second paragraph as indefinite. The Examiner cites several examples of alleged indefiniteness.

In the first place, the Examiner asserts that the terms “novel” and “known” in the preamble of claim 1 render the claim indefinite. Claim 1 has been amended herein by removal of the term “known” from the preamble and by repositioning of the word “novel” to more particularly point out the novelty that may be ascribed to the products of the claimed method. Again, the clarification of the “metes and bounds” of novelty is further enhanced in the addition by amendment herein of further steps (d) and (e) to the claimed method, and the “relative limitations” of the term “known” in step (d) would clearly be appreciated by one of skill in the art. This rejection is now moot and should be withdrawn.

The Examiner further asserts that the antecedent basis for the "amino acid secondary structural elements" recited in the steps of claim 1 is not clear from the language of the preamble. Again, the claim has been amended to make clear the relationship between the "backbone configurations" of the preamble and the "secondary structural elements" of the steps of the claim. The newly added steps complete the sequence of steps that are used to carry out the claimed method and make clear what original steps (a) through (c) are directed to.

Further in regard to step (a), the Examiner indicated during the interview her belief that language at the time did not make it clear that the number of each type of amino acid secondary structural element is fixed. The claim has been amended to further clarify this concept. Support for the amendment can be found on, for example, page 9, lines 1-3 of the specification. In the wake of this amendment, claims 5 and 6 have also been amended to avoid any possible issues of antecedent basis.

Claim 23 has been rejected for alleged indefiniteness of the definition of "n." The definition of the term has been amended herein to remove any possible ambiguity.

Claim 28 has been rejected for reciting "the average number of sequences per stack." Again, this is based on an alleged lack of antecedent basis. Applicants maintain, however, that the antecedent basis for the limitation is clear and that literal antecedent basis is not required in this instance. Although the concept of "average number of sequences per stack" is not literally recited in claim 1, it is clear from page 9, lines 21-25 of the specification that step (c) of claim 1 is performed by determining the number of amino acid sequences having a particular stack as their lowest energy conformation. From this, it is clear that step (c) of claim 1 allows for the determination of the number of sequences having each stack of a set of stacks as their lowest energy conformation and that from this an average can be determined and, accordingly, all stacks

which a larger-than-average number of sequences have as their lowest energy conformation can be identified. This concept has been reinforced by the addition of new steps (d) and (e) to the body of claim 1. Applicants respectfully submit that the rejection should be withdrawn.

V. Rejection under 35 U.S.C. §102

Claims 1-7, 15, 20, 23 and 24 stand again rejected under 35 U.S.C §102(b) as anticipated by the 1997 reference of Dahiyat et al. During the interview, the Examiners averred that the claims are broad enough to encompass at least one embodiment of Dahiyat.

The Examiner contends that various passages selected from Dahiyat teach each and every element of Applicants' invention as claimed. As Professor Wingreen carefully explained, and as can be gleaned from a careful reading of the applied reference, the Dahiyat process does not generate, or involve in any way, novel backbone configurations. Dahiyat starts with a previously known, and invariant, backbone configuration. Dahiyat then attempts to fit a new sequence of amino acids into that configuration. On this basis alone, the anticipation rejection is plainly without merit.

Furthermore, although claim 1 has been amended to address other issues raised by the Examiner and discussed above, the amendments also have the effect of further establishing the patentable distinction between Applicants' invention and Dahiyat.

The Examiner believes that the previous amendments to the preamble of claim 1 do not "give life, meaning and vitality" to the claim and has refused to give patentable weight to the amendment. This and the Examiner's various other observations are moot in light of the amendments to claim 1.

Applicants previously cited, for example, the Dahiyat disclosure on page 82, second column, first sentence under “Sequence selection” and Dahiyat Fig. 6 as supporting their contention that the method of Dahiyat is specifically aimed at identifying a new sequence of amino acids that will adopt a prespecified, previously known, and naturally occurring backbone configuration. The limitation of present claim 1 as amended herein that the claimed method produces novel backbone configurations is certainly part of the “life, meaning and vitality” of the claim and conveys an end result of the method that is not possible with the Dahiyat process.

Still further, the additional steps added to claim 1 not only contribute to the clarification of novelty with respect to the configurations generated by Applicants’ process, but the new steps recite additional aspects of the present invention that Dahiyat cannot be said to teach.

Anticipation requires that each and every element be identically disclosed in a single reference. The Examiner’s burden in this regard has not been carried. The Dahiyat passages cited in paragraphs 21-26 of the Office Action are all ultimately tied in with identification of alternative amino acid sequences for a prespecified, known backbone configuration. This is not the present invention as defined by the steps of claim 1. Furthermore, any specific techniques and/or parameters disclosed in these Dahiyat passages and used as a basis for rejection of dependent claims in the present application are applied to this same Dahiyat framework of working with a prespecified, known backbone configuration.

VI. Rejection under 35 U.S.C. §103

Claims 1-7, 9-11, 15, 16, 20, 23 and 24 remain rejected under 35 U.S.C. §103(a) as being obvious over the same 1997 reference of Dahiyat et al. in combination with U.S. Patent No. 6,403,312 to Dahiyat et al.

The amendments introduced herein and discussed above clearly show the differences between the claimed invention and the method disclosed in the primary Dahiyat reference and further make clear the deficiencies in that reference.

Although the Dahiyat article was first invoked as an anticipatory reference, in the obviousness rejection some deficiencies of the article are conceded. The Examiner contends that the Dahiyat patent as a secondary reference discloses features that are admittedly absent from the Dahiyat article. In summary, it is the Examiner's stated belief that the primary Dahiyat reference discloses the design of "stable, well-folded proteins with a fully automated novel sequence selection," that the secondary Dahiyat reference teaches "using a protein library" and "using the conjugate gradient method" and that the skilled artisan would have been motivated to combine these teachings. However, whether or not the Examiner's assertions are true regarding what the secondary reference teaches and regarding motivation to combine those teachings with those of the primary reference, combination of the teachings would not lead one of skill in the art to the instantly claimed invention.

As made clear above in Section V, among other shortcomings Dahiyat fails to disclose a means for identification of previously unknown, realizable backbone configurations. Furthermore, the Examiner's assessment in paragraph 21 of the Office Action that "Dahiyat et al. discloses a method for designing stable and well-folded (backbone configurations) proteins..." is simply without merit. Dahiyat discloses no means for designing protein backbone configurations, either known or novel. Again, these are fundamental flaws and render the primary reference ineffective as prior art.

The necessary disclosures are not found in the Dahiyat patent, either. Neither the alleged teaching of the secondary reference of the use of a protein library nor the specific teaching of the

use of a conjugate gradient method, also attributed by the Examiner to the secondary reference, furnishes the teaching that the Dahiyat article fails to provide. Accordingly, the Examiner has failed to meet the burden of establishing a prima facie case of obviousness. More particularly, the Examiner has failed to establish that the combination of the cited references would reasonably lead one of ordinary skill in the art to the claimed invention. Thus, regardless of considerations of motivation to combine what teachings are truly available to the skilled artisan via the two references, the rejection cannot stand and should be withdrawn.

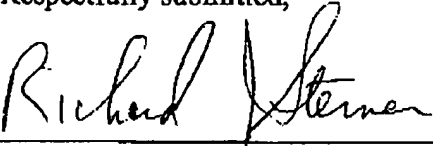
VII. Conclusion

The amendments to the claims have addressed the nonstatutory subject matter, new matter and enablement issues raised by the Examiner. Furthermore, the combination of claim amendments and arguments presented above set forth the patentable distinction between the claimed invention and the teachings of the cited references. Reconsideration and allowance of the application with pending claims 1-25 and 28 are respectfully requested. Should any other matters require attention prior to allowance of the application, it is requested that the Examiner contact the undersigned.

No additional fees should be due in connection with this communication. However, should it be determined that an additional fee is due for any reason, the Commissioner is hereby authorized to charge it to Deposit Account No. 23-1703.

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Respectfully submitted,


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